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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,971	10/04/2001	Muthiah Manoharan	ISIS-4789	3195
32650	7590	10/20/2004	EXAMINER	
WOODCOCK WASHBURN LLP ONE LIBERTY PLACE - 46TH FLOOR PHILADELPHIA, PA 19103			OWENS JR, HOWARD V	
			ART UNIT	PAPER NUMBER
			1623	
DATE MAILED: 10/20/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

### Application No.

09/970,971

### Applicant(s)

MANOHARAN ET AL.

### Examiner

Howard V Owens

### Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-13, 18 and 21-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-13, 18 and 21-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### ***Response to Arguments***

The following is in response to the amendment filed 6/7/04

An action on the merits of claims 1-14 and 29-41 is contained herein below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### **Double Patenting**

Applicant's arguments have been fully considered but they are not persuasive. The rejection of claims 1-13, 18 and 21-32 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,369,209 in view of Damha et al., Bioconjugate Chem., Vol. 10, 1999, pages 299-305 is maintained for the reasons of record set forth below.

Instant Claims 1-13, 18 and 21-32 are drawn to an oligonucleotide containing A-form and B-form 2' substituted nucleotides.

Claims 1-25 of '209 are drawn to analogous oligonucleotide; however, the B-form of the first portion contains at least 2 arabinonucleotides.

Damha teaches that the substitution of arabinose as the pentosyl moiety confers more stability to serum and cellular nucleases than DNA.

It would have been prima facie obvious to substitute an arabinose as the pentosyl moiety in a duplex oligonucleotide.

One of skill in the art would have been motivated to substitute an arabinose as the pentosyl moiety in a duplex oligonucleotide to provide even greater resistance to nuclease attack. Applicant has not provided a response to the motivation provided by the teachings of Damha to substitute an arabinose sugar for ribose.

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35 USC 102

Applicant's arguments have been fully considered but they are not persuasive. The rejection of claims 1, 2, 3, 5 – 9, 18, 21-29 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Cook et al., U.S. Patent No. 5, 670,633 is maintained for the reasons of record set forth below.

Claims 1 is drawn to an oligonucleotide comprising a plurality of nucleotides, wherein a first portion of said plurality of nucleotides have continuous B-form geometry and continuous A-form geometry.

Dependent claims 2, 3, 5-9, 18, 21-29 are drawn to a 2' fluoro substituent present at the nucleotides, wherein the nucleosides are linked through phosphorothioate or methyl phosphonate linkages.

Cook teaches an oligonucleotide that hybridizes with RNA or DNA, which inherently confers A and B conformational geometry wherein the nucleotides are ribonucleotides (see column and claims 1-3), wherein deoxy and ribose sugars are present in the oligonucleotide chain, and at least two of said nucleosides include a modified deoxyfuranosyl moiety bearing a 2' fluoro substituent. Cook also teaches the use of phosphorothioate or methyl phosphonate linkages between the nucleosides (column 7, line 65 – column 8, line 2 and claim 3).

Applicant asserts that the claimed structure is not present in Cook; however, there is no response to the examiner's argument that cited supra that the claimed structure is inherently taught through the oligonucleotide that hybridizes with RNA or DNA, which inherently confers A and B conformational geometry wherein the nucleotides are ribonucleotides (see column and claims 1-3), wherein deoxy and ribose sugars are present in the oligonucleotide chain, and at least two of said nucleosides include a modified deoxyfuranosyl moiety bearing a 2' fluoro substituent.

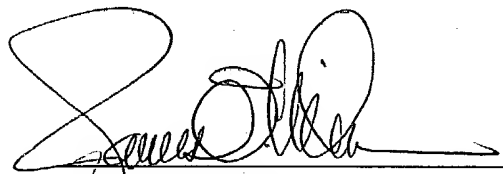
For the reasons set forth supra, the rejections of record are maintained

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**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Howard V. Owens  
Patent Examiner  
Art Unit 1623



James O. Wilson  
Supervisory Patent Examiner  
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (571) 272-0658. The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (571) 272-0661.